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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,249	02/06/2006	Paul J. Coleman	21484P	2287

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EXAMINER	
COLEMAN, BRENDA LIBBY	
ART UNIT	PAPER NUMBER
1624	
MAIL DATE	DELIVERY MODE
03/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,249	COLEMAN ET AL.	
	Examiner	Art Unit	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,20-23,27,28 and 30-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5* is/are allowed.

6)☒ Claim(s) *1-4,6-10,20-23,27,28 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10, 20-23, 27, 28 and 30-33 are pending in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 7-10, 20-23, 27, 28 and 30-33 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The scope of the method claims is not adequately enabled solely based on inhibiting the growth of a proliferating cell provided in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The scope of these claims call for the treatment of cancer. However, there never has been a compound capable of treating cancer generally. There are compounds that treat a range of cancer, but no one has ever been able to figure out how to get a compound to treat cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective anti-tumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco

tars, genetic disorders, ionizing radiation, and a wide variety of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task.

Instant claim language embraces disorders not only for treatment but also for prevention, which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop cancer. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See In re Ruskin, 148 USPQ 221; Ex parte Jovanovics, 211 USPQ 907; MPEP 2164.05(a).

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. Genentech Inc. v. Novo Nordisk 42 USPQ2d 1001.

2. Claims 21-23, 27, 28, 30 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains

subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the instant invention has claims which embrace dihydropyrroles. The pharmaceutical compositions of the instant invention where an additional active ingredient such as 1) an estrogen receptor modulator, 2) an androgen receptor modulator, 3) a retinoid receptor modulator, 4) a cytotoxic/cytostatic agent, 5) an antiproliferative agent, 6) a prenyl-protein transferase inhibitor, 7) an HMG-CoA reductase inhibitor, 8) an HIV protease inhibitor, 9) a reverse transcriptase inhibitor, 10) an angiogenesis inhibitor, 11) PPAR-γ agonists, 12) PPAR-δ agonists, 13) an inhibitor of inherent multidrug resistance, 14) an anti-emetic agent, 15) an agent useful in the treatment of anemia, 16) an agent useful in the treatment of neutropenia, 17) an immunologic-enhancing drug, 18) an inhibitor of cell proliferation and survival signaling, 19) an agent that interfers with a cell cycle checkpoint, 20) paclitaxel, 21) trastuzumab, 22) a proteosome inhibitor, 23) aurora kinase inhibitor, 24) serine/threonine kinase inhibitor, and 25) an inhibitor of a mitotic kinesin that is not KSP are included in the

compositions. The specification does not define that which is intended in the additional active ingredients, i.e. which an estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an H1V protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, PPAR-γ agonists, PPAR-δ agonists, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, and an agent that interfers with a cell cycle checkpoint, paclitaxel, trastuzumab, a proteosome inhibitor, aurora kinase inhibitor, serine/threonine kinase inhibitor, an inhibitor of a mitotic kinesin that is not KSP, etc.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4, 6-10, 20-23, 27, 28 and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by Hydrogen in the definition of R^3 which begins with a capital letter indicating the beginning of the claim which is not so.

b. Claims 1, 2 and claims dependent thereon recite the limitation "alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three

substituents selected from R^{7}" in the definition of R^4. There is insufficient antecedent basis for this limitation in the claim.

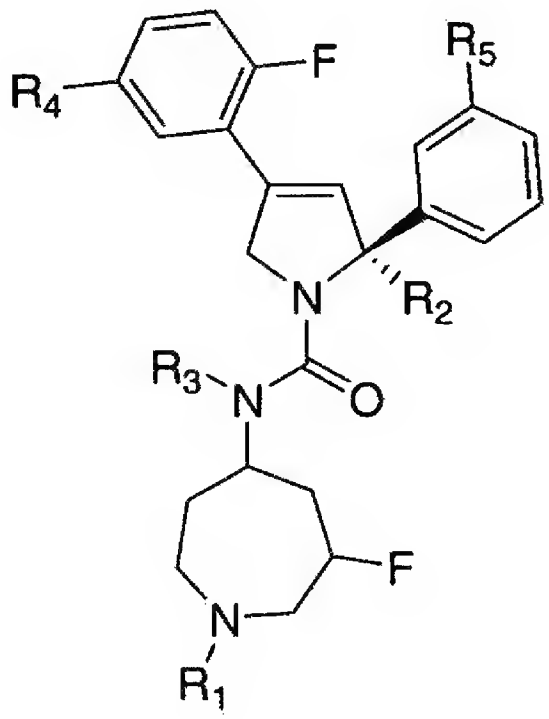
c. Claims 1, 2 and claims dependent thereon recite the limitation "alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R^{7}" in the definition of R^5. There is insufficient antecedent basis for this limitation in the claim.

d. Claims 1, 2, 3, 4 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of R^b where R^b is H, ... optionally substituted with one, two or three substituents selected from R^7.

e. Claims 1, 2, 3, 4 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of R^e and $R^{e'}$ where R^e and $R^{e'}$ are independently selected from: H, ... optionally substituted with one, two or three substituents selected from R^7.

f. Claim 1 is vague and indefinite in that it does not end with a period indicating the end of the claim.

g. Claim 6 recites the structural formula

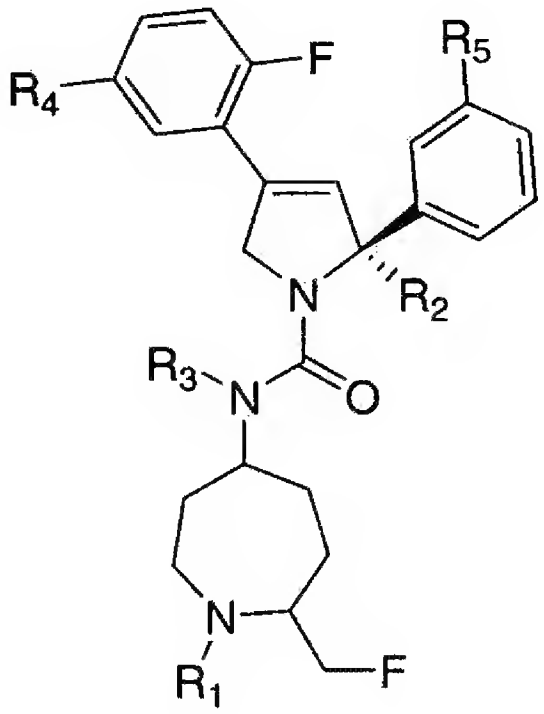


on page 20. There is insufficient antecedent basis for this limitation in the claim. Applicants' attention is directed to 1) the point of attachment of the R_2 and the R_5 substituted phenyl; 2) the use of subscripts rather then superscripts which are used in claim 1 from which claim 6 depends; 3) the use of different variables such as R_2 where in Formula I the variable is an R^3, R_3 where in Formula I the variable is an R^1; R_1 where in Formula I the variable is an R^2, etc.

h. Claim 6 recites the limitation "NO_2" in the definition of R_4 on page 27. There is insufficient antecedent basis for this limitation in the claim.

i. Claim 6 recites the limitation "SH" in the definition of R_5 on page 27. There is insufficient antecedent basis for this limitation in the claim.

j. Claim 6 recites the structural formula

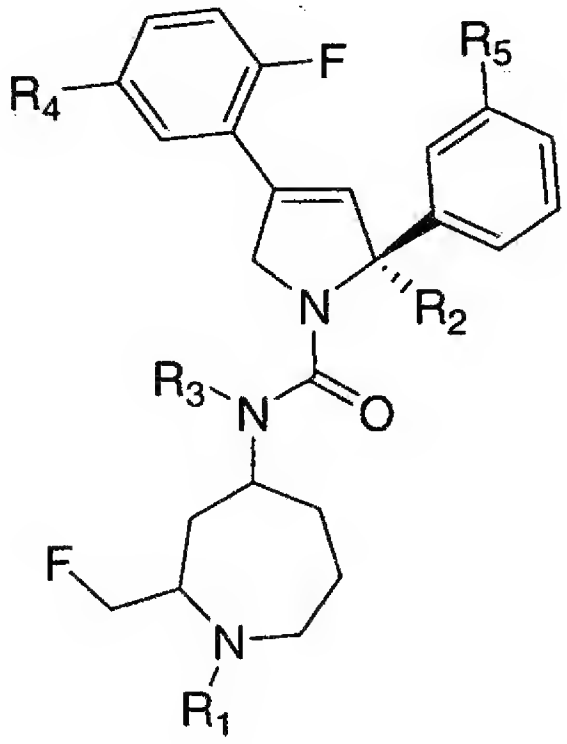


k. on page 28. There is insufficient antecedent basis for this limitation in the claim. Applicants' attention is directed to 1) the point of attachment of the R_2 and the R_5 substituted phenyl; 2) the use of subscripts rather then superscripts which are used in claim 1 from which claim 6 depends; 3) the use of different variables such as R_2 where in Formula I the variable is an R^3, R_3 where in Formula I the variable is an R^1; R_1 where in Formula I the variable is an R^2, etc.

l. Claim 6 recites the limitation "NO_2" in the definition of R_4 on page 35. There is insufficient antecedent basis for this limitation in the claim.

m. Claim 6 recites the limitation "SH" in the definition of R_5 on page 35. There is insufficient antecedent basis for this limitation in the claim.

n. Claim 6 recites the structural formula

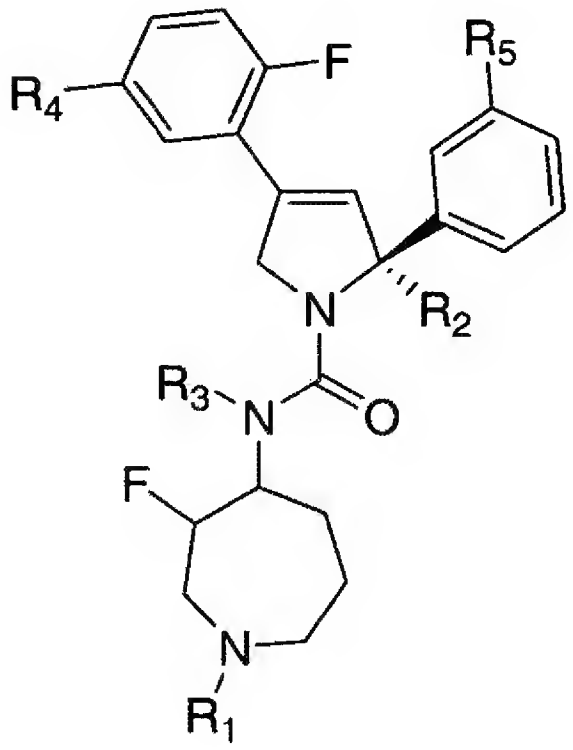


o. on page 36. There is insufficient antecedent basis for this limitation in the claim. Applicants' attention is directed to 1) the point of attachment of the R_2 and the R_5 substituted phenyl; 2) the use of subscripts rather then superscripts which are used in claim 1 from which claim 6 depends; 3) the use of different variables such as R_2 where in Formula I the variable is an R^3, R_3 where in Formula I the variable is an R^1; R_1 where in Formula I the variable is an R^2, etc.

p. Claim 6 recites the limitation "NO_2" in the definition of R_4 on page 43. There is insufficient antecedent basis for this limitation in the claim.

q. Claim 6 recites the limitation "SH" in the definition of R_5 on page 43. There is insufficient antecedent basis for this limitation in the claim.

r. Claim 6 recites the structural formula



on page 44. There is insufficient antecedent basis for this limitation in the claim. Applicants' attention is directed to 1) the point of attachment of the R_2 and the R_5 substituted phenyl; 2) the use of subscripts rather then superscripts which are used in claim 1 from which claim 6 depends; 3) the use of different variables such as R_2 where in Formula I the variable is an R^3, R_3 where in Formula I the variable is an R^1; R_1 where in Formula I the variable is an R^2, etc.

s. Claim 6 recites the limitation "NO_2" in the definition of R_4 on page 51. There is insufficient antecedent basis for this limitation in the claim.

t. Claim 6 recites the limitation "SH" in the definition of R_5 on page 51. There is insufficient antecedent basis for this limitation in the claim.

u. Claim 10 is vague and indefinite in that it is not known what is meant by gioblastomas.

v. An estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an H1V protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, PPAR-γ agonists, PPAR-δ agonists, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, and an agent that interfers with a cell cycle checkpoint, a proteosome inhibitor, aurora kinase inhibitor, serine/threonine kinase inhibitor, an inhibitor of a mitotic kinesin that is not KSP in claims 21, 22, 27, 28, 30 and 31 are relative terms, which renders the claim indefinite. The specific terms of claims 21, 22, 27, 28, 30 and 31 "estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an H1V protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, PPAR-γ agonists,

PPAR-δ agonists, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, and an agent that interfers with a cell cycle checkpoint, a proteosome inhibitor, aurora kinase inhibitor, serine/threonine kinase inhibitor, an inhibitor of a mitotic kinesin that is not KSP" are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The nature of the composition consisting of the compounds of formula I and an additional active ingredient, which is an estrogen receptor modulator, an androgen receptor modulator, a retinoid receptor modulator, a cytotoxic/cytostatic agent, an antiproliferative agent, a prenyl-protein transferase inhibitor, an HMG-CoA reductase inhibitor, an H1V protease inhibitor, a reverse transcriptase inhibitor, an angiogenesis inhibitor, PPAR-γ agonists, PPAR-δ agonists, an inhibitor of inherent multidrug resistance, an anti-emetic agent, an agent useful in the treatment of anemia, an agent useful in the treatment of neutropenia, an immunologic-enhancing drug, an inhibitor of cell proliferation and survival signaling, and an agent that interfers with a cell cycle checkpoint, a proteosome inhibitor, aurora kinase inhibitor, serine/threonine kinase inhibitor, an inhibitor of a mitotic kinesin that is not KSP.

Allowable Subject Matter

4. Claim 5 is allowed. None of the prior art of record or a search in the pertinent art area teaches the compounds as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brenda L. Coleman/
Primary Examiner, Art Unit 1624